

In the Claims:

Please amend claim 9 as follows:

1.(withdrawn) A method of *in vitro* screening for a ligand including selecting said ligand by means of at least two assay systems, said method comprising the steps of:

a) in a cellular or tissue assay system comprising an estrogen receptor and an estrogen receptor-driven reporter gene, selecting the ligand having a transcriptional activity mediated by activation of the estrogen receptor and measured by detecting a potency in the cellular or tissue assay system, whereby in the cellular or tissue assay system the ligand activates the potency with a half-maximally effective ligand concentration

(EC₅₀(ER)) less than or equal to 10 nmol/l, and

detecting the activation of the transcription;

and

b) in a cell-free or enzymatic assay system, selecting a physical-chemical interaction of a co-present steroid receptor coactivator-1, and fragments thereof, and the estrogen receptor, which is measured by detecting a potency of said interaction in the cell-free or enzymatic system, wherein the ligand activates the estrogen receptor and induces said interaction with said co-present steroid receptor coactivator-1, and fragments thereof, in the cell-free or enzymatic assay system with a half-

maximally effective ligand concentration ($EC_{50}(ER+SRC)$) greater than or equal to 100 nmol/l, and detecting a potency of the physical - chemical interaction of the co-present steroid receptor coactivator-1, and fragments thereof, and the estrogen receptor.

2. (withdrawn) A method of *in vitro* screening for a ligand, said ligand being an estrogen or having estrogenic activity, in a cell-free or enzymatic assay system by selecting a physical-chemical interaction of a co-present steroid receptor coactivator-1, and fragments thereof, and an estrogen receptor, said physical-chemical interaction being measured by detecting a potency of said interaction in the cell-free or enzymatic assay system,

wherein the ligand activates the estrogen receptor and induces said interaction with the co-present steroid receptor coactivator-1, and fragments thereof, in the cell-free or enzymatic assay system with a half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) greater than or equal to 100 nmol/l, and detecting the potency of the physical-chemical interaction of said co-present steroid receptor coactivator-1, and fragments thereof, and of said estrogen receptor.

3.(withdrawn) A method of *in vitro* screening according to claim 2, wherein said ligand is said estrogen and transcriptionally activates a cellular assay system comprising said estrogen receptor and an estrogen-receptor-driven reporter

gene, wherein the ligand activates a potency with a half-maximally effective ligand concentration ($EC_{50}(ER)$) less than or equal to 10 nmol/l.

4.(withdrawn) A method of *in vitro* screening for one or more ligands from a group of test substances, said test substances being selected from the group consisting of estrogens and compounds having estrogen activity, said method comprising the steps of:

a) providing a cell-free or enzymatic assay system for each of said test substances, said cell-free or enzymatic assay system comprising an estrogen receptor for said test substances and a co-present steroid receptor coactivator-1, and fragments thereof.

b) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER+SRC)$) for each of said test substances at which a physical-chemical interaction of said co-present steroid receptor coactivator-1, and said fragments thereof, and said estrogen receptor occurs in the cell-free or enzymatic system in the presence of each of said test substances; and

c) selecting said one or more ligands from said group of test substances if said half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) for said one or more ligands is greater than or equal to 100 nmol/l.

5.(withdrawn) The method as defined in claim 4, wherein said physical-chemical interaction is detected by experimentally measuring fluorescence energy transfer

between a fluorescently-labeled steroid receptor coactivator-1 and a fluorescently-labeled nuclear receptor.

6.(withdrawn) The method as defined in claim 4, wherein said one or more ligands are from said estrogens and transcriptionally activate a cellular assay system at half-maximally effective ligand concentrations less than or equal to 10 nmol/l, wherein said cellular assay system comprises said estrogen receptor and an estrogen-receptor-driven reporter gene.

7.(previously presented) A method of screening a group of test substances for one or more ligands to be administered as effective ingredients in a method of treating neuro-degeneration, said test substances being selected from the group consisting of estrogens and compounds having estrogen activity, said method of screening comprising the steps of:

a) providing a cell-free or enzymatic assay system for each of said test substances, said cell-free or enzymatic assay system comprising an estrogen receptor for said test substances and a co-present steroid receptor coactivator-1, and fragments thereof;

b) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER+SRC)$) for each of said test substances at which a physical-chemical interaction of said co-present steroid receptor coactivator-1, and said fragments thereof, and said estrogen receptor occurs in the cell-free or enzymatic system in the presence of each of said test substances;

c) selecting said one or more of said test substances if said half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) for said one or more of said test substances is greater than or equal to 100 nmol/l;

d) providing a cellular or tissue assay system comprising an estrogen receptor and an estrogen receptor-driven reporter gene;

e) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER)$) for said one or more test substances selected during the selecting of step c); at which said cellular or tissue assay system is transcriptionally activated in the presence of said one or more test substances; and

f) selecting those of said one or more test substances having said half-maximally-effective ligand concentrations that transcriptionally activate said cellular or tissue assay system and that are less than or equal to 10 nmol/l as said one or more ligands for said method of treating said neuro-degeneration.

8.(withdrawn) A method of treating neuro-degeneration in cerebral cortex of a human being, said method comprising the step of administering an effective amount of 3',15 β -dihydrocycloprop[14,15]-estra-1,3,5(10),8-tetraene-3,17 α -diol of said human being.

9.(currently amended) A method of screening a group of test substances for one or more ligands to be administered as effective ingredients in a method of treating neuro-degeneration, said test substances being selected from the group

consisting of estrogen; and compounds having estrogen activity, said method of screening comprising the steps of:

a) providing a cell-free or enzymatic assay system for each of said test substances, said cell-free or enzymatic assay system comprising an estrogen receptor for said test substances and a co-present steroid receptor coactivator-1, and fragments thereof;

b) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER+SRC)$) for each of said test substances at which a physical-chemical interaction of said co-present steroid receptor coactivator-1, and said fragments thereof, and said estrogen receptor occurs in the cell-free or enzymatic system in the presence of each of said test substances;

c) selecting said one or more of said test substances if said half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) for said one or more of said test substances is greater than or equal to 100 nmol/l;

d) providing a cellular or tissue assay system comprising an estrogen receptor and an estrogen receptor-driven reporter gene;

e) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER)$) for said one or more test substances selected during the selecting of step c); at which said cellular or tissue assay system is transcriptionally activated in the presence of said one or more test substances; and

f) selecting those of said one or more test substances having said half-maximally-effective ligand concentrations that transcriptionally activate said

cellular or tissue assay system and that are less than or equal to 10 nmol/l as said one or more ligands for said method of treating said neuro-degeneration;

~~The method as defined in claim 7 or 8, wherein~~

wherein said neuro-degeneration is an age-related cognitive disorder, affective disorder, Alzheimer's disease or cerebral ischemia/stroke.